JERRY W. BUSH, M.D.

Board Certified Internal Medicine
B.S. Law B.S. Pharmacy
Certified Independent Medical Examiner
Certified Medical Review Officer
Medical Expert Witness
Civil, Criminal & Administrative
Medical-Legal Consulting
Medical Pharmacology
Social Security Disability Examinations

686 South 8th Street
Griffin, GA 30223

8 September 2009

MEDICAL-PHARMACOLOGIC ANALYSIS IN RE:

Savannah Hill vs. Sanofi-Aventis Pharmaceuticals, Inc.

Loudon County, Virginia

PURPOSE: The purpose of this report is to review the medical-pharmacologic issues relating to Savannah and her mother, Janelle Hill, in the prenatal and postnatal periods.

QUALIFICATIONS

I am qualified to offer such medical opinions due to my education, training and experience. I was graduated from the University of Alabama School of Medicine in Birmingham, AL and the Auburn University School of Pharmacy in Auburn, AL, where I received the President's Award as the number one graduate for the year. I have taken courses in medicinal chemistry, pharmacokinetics, drug analysis and pharmacology. I then became a Diplomat of the American Board of Internal Medicine. I attained qualification as a Certified Medical Review Officer (CMRO), which relates to special expertise in the analysis of drug tests. I have in the past attained qualification as a Certified Independent Medical Examiner (CIME), which relates to special expertise in the performance of disability/impairment examinations. Over the past 20 years, I have performed approximately 10,000 evaluations, relating to assessment of a patient's ability to engage in gainful full-time employment. I have attained DEA certification for the prescribing of the drug buprenorphine, used in the outpatient treatment of opiate dependency. I have been certified as an expert in pharmacology by both state and federal courts. Finally, I have practiced medicine for over 20 years.

I have been certified by courts to offer expert testimony as to the effects of anticoagulants on an infant. I testified in the case of *State of Florida vs. Yurko,* which involved issues of pharmacology/toxicology/physiology of anticoagulants related to an infant.

CASE SYNOPSIS

Savannah Hill was born on 07.27.2003 at the Loudoun Hospital Center, with a birthweight of 2774 grams and a gestational age of 40 weeks. The delivery was vaginal/vertex. Intrauterine growth was deemed AGA (average for gestational age). Apgar scores were 2 at one minute and 9 at 5 minutes. The infant was Rh negative and Coombs positive. The ABO blood type was O. Savannah was transferred to Inova Fairfax Hospital due to the onset of seizures occurring at 20 hours. Seizure activity recurred 8 hours later notwithstanding the administration of phenobarbital. A brain CT scan revealed parenchymal-subarachnoid-subdural bleeding, along with a vitreous hemorrhage. Oxygen saturations dropped to the mid-80s during the transfer.

Her mother was 30-years-old at this time being Gravada 4 Para 1. Her blood type was O. The maternal prenatal screening included negative tests for group B strep, hepatitis B and serologic test for syphilis. Maternal medications included enoxaparin (Lovenox®). The mother experienced a deep vein thrombosis (DVT) during the fourth month of gestation. At that time she was placed on a heparin drip for 4 days followed by a course of Lovenox® bid for the remainder of her pregnancy. Three days before delivery, the Lovenox® was discontinued and then restarted after the delivery. The infant was given vitamin K, and ampicillin/ gentamycin were administered for a rule out sepsis indication. Savannah was found to be thrombocytopenic at 31 K and was transfused with platelet concentrate. Complications included meconium stained amniotic fluid and decelerations.

Janelle Hill underwent a RLE venous Doppler at Reston Hospital in Reston, VA on 02.19.2003, with an indication of "Right leg cramping, Rule out DVT." The study was read as "DVT popliteal vein extending into the deep veins of the calf."

The in-hospital diagnoses of Savannah Hill were as follows:

(1) Intraventricular hemorrhage newborn/fetus, Grade II
(2) Convulsions in newborn
(3) Transient neonatal thrombocytopenia
(4) Hemolytic disease newborn/fetus
(5) Hypocalcemia/hypomagnesemia newborn
(6) Cerebral thrombosis/infarction
(7) Hyperkalemia
(8) Unspecified hearing loss
(9) Stridor
(10) Vitreous hemorrhage

According to the complaint, the "factual background"

is as follows:

1. On or about July 27, 2003, Plaintiff Janelle B. Hill was admitted to Defendant Loudoun Hospital Center's Birthing Inn because she had gone into labor with her unborn child.
2. During the time period of labor, the fetal heart monitor reflected that the infant was in fetal distress.
3. Upon delivery, the infant, Plaintiff Savannah Hill, suffered from hypoxia, abnormal PT/ PTT levels, thrombocytopenia and intraventricular cranial bleeds, ultimately causing severe and extensive neurological damage, leading to permanent disabilities.
4. After the delivery, Plaintiff Savannah Hill, underwent three separate blood transfusions.
5. Plaintiff Savannah Hill was transferred to INOVA Fairfax Hospital on July 28, 2003.

EVIDENCE REVIEWED

(1) INOVA Fairfax Hospital medical records
(2) Complaint
(3) Aventis Pharmaceuticals Letter
(4) FDA Medwatch
(5) Loudoun records
(6) Costs to date table
(7) Liftetime costs projection tables
(8) Lifetime costs of equipment and medical evaluations tables
(9) Noted journal articles
(10) Janelle Hill prenatal medical records

KHURRAM RASHID, M.D. OFFICE NOTES

The notes indicated that Janelle Hill's Estimated Date of Delivery was 07.27.2003. The identified "Problems/Plans" included (1) H/O DVT x 2, presently on Lovenox® and (2) Will D/C 24 hours prior to induction. The notes indicated that she had experienced an episode of a popliteal DVT in 07.29. 2002. She had been on Coumadin® until 2002. She subsequently experienced another episode of DVT in the right leg on 10.30.2002. On 02.20.2003, she had a venous doppler that revealed: "Deep vein thrombosis involving the distal superficial femoral and popliteal veins. Findings are of concern for slight proximal propagation of thrombus since the previous study into the distal SFV." On 03.03.2003, she underwent a right lower extremity venous Doppler, which revealed "Resolution of right lower extremity DVT." Ms. Hill underwent a CT angiogram of the chest on 10.24.2003, with the impressions of: (1) RLL pulmonary embolus and (2) Two nodular opacities at the left lung base that may represent areas of atelectasis or pulmonary infarction.

AVENTIS LETTER 07.20.2004:

On this date, the Aventis™ Pharmaceutical Company wrote a letter to Dr. Khan. Dan Wozinski, R.Ph. wrote that "In an ongoing effort to increase our knowledge pertaining to the use of Lovenox during pregnancy, we are requesting that you provide us with additional patient information…" The information requested included the following:

(a) Patient demographics
(b) Additional information describing the adverse event including symptoms, time of onset, CBC, blood chemistry, SrCr, anti-Xa level, PT, aPTT, INR, etc. for mother & child
(c) Therapy dates
(d) Remedial measures and treatment of the event
(e) Outcome
(f) Relationship between this event and Lovenox®
(g) Concomitant medications including OTC medications (mother)
(h) Medical & surgical history, social history, history of STD, environmental exposures, occupation, pregnancy history, etc.

NEUROLOGY CONSULTATION

Baby girl Savannah Hill underwent a neonatal neurology consultation at the Inova Fairfax Hospital for Children by Sylvia Mandler, M.D. on 07.30.2003. The history noted was as follows: "…presented with neonatal seizures at 18 hours of life…head CT was consistent with bilateral intraventricular hemorrhages and some limited collections of blood in the parenchyma

and subarachnoid hemorrhage. Her electroencephalogram was remarkable for sharp activity predominantly on the right side, and sharp and slow waves…loaded with Phenobarbital and has been seizure free for several hours with a level of 46…undergoing an extensive hematological workup to elucidate the etiology of this intracranial bleed…mother had a history of a deep venous thrombosis during pregnancy for which she was treated with Lovenox throughout the pregnancy." Dr. Mandler further related that the patient would be at increased risk for hydrocephalus and should receive periodic brain imaging.

There is another neurology consultation by Dr. Mandler dated 07.30.2003. The noted history is as follows: "…baby's mother…experienced deep venous thrombosis (DVT) during the fourth month of her gestation. At that time she was placed in a heparin drip for four days and then she was started on Lovenox twice a day until the end of the pregnancy. Three days prior to her delivery, the Lovenox was put on hold and it was restarted after the baby was born…found to be thrombocytopenic…"

HEMATOLOGY CONSULTATION

Savannah Hill underwent a hematology consultation on 08.01.2003 by Marcie Weil, M.D. The consultant was again asked to see the patient and to elucidate the cause of her thrombocytopenia. The baby had already received cryoprecipitate and platelets. She had also been given IV IgG. The clotting factors II, VIII and IX were performed and were found to be normal. The plan was to study the mother's blood to see if it agglutinates the father's blood. Also planned was to check the level of heparin-induced platelet activator antibody. On 07.30.2003, Savannah's platelet count was decreased to 112 K. On July 29th, a hematologist's impression was: "Thrombocytopenia, possibly due to DIC vs clot vs alloimmune coagulopathy." A "*suspected* diagnosis" was a "minor blood group incompatibility."

The infant's first platelet count at Loudon Hospital drawn after the first seizure was 45 K. The mother's ANA and anti-phospholipid antibody were negative. The von Willebrand antigen was 142 (reportedly normal). The brain imaging studies showed clots in the sagittal sinus, raising the possibility of possible "thrombotic" etiologies.

FDA MEDWATCH: FDA MEDICAL PRODUCTS REPORTING PROGRAM:

Aventis® Pharmaceuticals, Inc. filed this report with the FDA on 07.19.2004. The date of the reported event was 07.28.2003. The narrative of this event was: "Initial report 15-Jul-2004, this spontaneous post-marketing case from the United States was reported by a physician and involves a newborn patient…patient's mother received enoxaparin 90 mg twice daily from the third to seventh month of pregnancy…" The reported events included (1) Subarachnoid hemorrhage, (2) Intraventricular hemorrhage, (3) Hypoacusis, (4) Eye hemorrhage and (5) Thrombocytopenia. The "Outcomes" attributed to adverse event included: (1) Lift-threatening, (2) Hospitalization, (3) Disability and (4) Required intervention to prevent permanent impairment/damage.

HEPARIN & LOW-MOLECULAR WEIGHT HEPARIN:

According to a 1998 article in the journal *Chest,* "Like unfractionated heparin, low molecular weight heparin produce their major anticoagulant effect by activating antithrombin…" (*Chest,* "Heparin and Low-Molecular-Weight Heparin," Hirsh, et al., 114:489S, Supplement pp 489S-510S. 1998) Also, according to this journal article, "Thrombocytopenia is a well-recognized complication of heparin therapy. Two forms of thrombocytopenia are described: an early benign, reversible nonimmune thrombocytopenia and a late, more serious IgG-mediated immune thrombocytopenia.

HEPARIN-INDUCED THROMBOCYTOPENIA (HIT) FURTHER DISCUSSION:

Definition

Heparin-induced thrombocytopenia (HIT) is a transient, immunologically-mediated, autoimmune -like, adverse drug reaction to exposure to heparin, including even exposure to minimal amounts of heparin (*e.g.,* flushes) (1).This reaction is due to antibodies against immune complexes consisting of a "self" protein, platelet factor 4 (PF4), and heparin. The antibodies activate platelets via their Fcγ receptors; this platelet activation is what, paradoxically, leads to thrombosis. (2).

HIT is defined as any clinical event best explained by platelet activating antiPF4/heparin antibodies (HIT antibodies) in a patient receiving or who recently received heparin. (3) HIT is a clinicopathologic syndrome. Thrombocytopenia is the most common clinical event, representing 90%, and thrombosis will develop in most patients with HIT.

Hirsch, *et al,* describe 2 distinct forms of HIT:

Type I : This type is non-immunologically-mediated and is an early benign form. Up to 15% of patients who receive heparin experience an acute thrombocytopenia that resolves spontaneously and has limited clinical sequelae. This is due to platelet clumping and/or transient sequestration of platelets.

Type II: This type is the classic, dangerous, immunological mediated form of HIT. It is due to the heparin-associated anti-platelet antibodies described above. This type develops in 1%-3% of patients taking UFH and 0.1%-0.5% 0f patients receiving LMWH.

In most instances, the diagnosis of HIT requires one or more clinical events (e.g. thrombocytopenia, thrombosis) with a temporal relationship of some sort with heparin exposure, with resultant pathologic HIT antibody formation (4).

Pathogenesis

The central concept in the pathogenesis of HIT is the formation of heparin dependent IgG that activates platelets through their Fcy Iia receptors. The target antigen is an immune complex

between anionic heparin and cationic PF4, a tetrameric member of the CXC subfamily of chemokines.5 HIT antibodies recognize altered sites on PF4.

Factors leading to thrombosis formation in HIT are primarily platelet activating nature of HIT antibodies, pan-cellular activation of endothelium and monocytes and neutralization of the anticoagulant effect of heparin by PF4 released from activated platelets (6).

Frequency

Four factors affect the frequency of HIT:

1. Duration of heparin use
2. Type of heparin
3. Type of patient population
4. Patient gender

Duration of heparin use (>1 week versus <1 day)	OR estimated as follows: risk for HIT postcardiac surgery (with UFH prophylaxis for >1 week) ~2% versus risk for "delayed-onset HIT" (without prophylaxis) ~0.02–0.1%
Type of heparin (UFH > LMWH)	Difference in risk for HIT between heparin types is established for postsurgical thromboprophylaxis (UFH versus LMWH) and is more pronounced in women.
Type of patient (surgery > medical > pregnancy)	Highest reported frequencies of HIT are in postsurgical thromboprophylaxis [18]
Gender (female > male)	Difference in risk for HIT between women and men has only been established for UFH thromboprophylaxis [18]

Clinical Picture

HIT is a distinct syndrome all its own when compared to other drugs that cause thrombocytopenia such as quinine, Vancomycin, and glycoprotein IIb/IIIa antagonists. Whereas

these other drugs cause severely low platelet counts and mucocutaneous hemorrhage, HIT only causes a relatively moderate decrease in platelet count and paradoxically thrombosis rather than hemorrhage. Also, although these other drugs cause dramatic bleeding, fatalities are quite rare. This is not the case with HIT, where fatalities and long term sequelae are relatively common and represent the usual outcome of a patient with HIT. HIT occurs more frequently than all other drug -induced causes of thrombocytopenia *combined.*

Thrombocytopenia

The median platelet count nadir is 60 x 10^9/L. Most patients have a 50% decrease in the platelet count. In post op patients, the baseline platelet count is not the preop platelet count but rather is the highest post op platelet count preceding the HIT associated platelet count decrease. A diagnosis of HIT is usually based on a fall in platelet count below 150. However, this definition may be inappropriate for post op patients who often develop post op thrombocytosis. The improved definition of HIT is a 50% or greater platelet count fall from the post op period.

"Typical onset" HIT (70% of patients) manifests as a platelet count decrease which begins 5-10 days after starting a course of heparin (1st day of heparin =day 0) with a median of 2 days required to reach a threshold defining thrombocytopenia.

"Rapid onset" HIT (25% of patients) is defined as thrombocytopenia which develops within 24 hours of exposure to heparin. This happens because the patient already has circulating HIT antibodies as a result of having been exposed to heparin in the preceding few weeks or months.

"Delayed onset" HIT is when the platelet count begins its descent after all heparin has been stopped.

Clinical Scoring System for HIT

In evaluating a patient for possible HIT, a clinical scoring system can help [33]. One system, the 4 Ts (Table 3), evaluates Thrombocytopenia, its Timing, the presence of Thrombosis (or other sequelae of HIT), and whether other plausible explanations for thrombocytopenia or thrombosis are present. A low score (=3 points) makes HIT unlikely (<2%). In some settings, a high score predicts a high likelihood of HIT.

Timing #[a] of platelet count decrease, thrombosis, or other sequelae (first day of heparin course = day 0) Score = _____	Day 5–10 onset#[a] or =1 day (with recent heparin exposure within past 5–30 days)	Consistent with day 5–10 decrease, but not clear (eg, missing platelet counts), or =1 day (heparin exposure within past 31–100 days), or platelet decrease after day 10	Platelet count decrease =4 days without recent heparin exposure

Thrombosis

The strong association between HIT and thrombosis and the tendency for thrombotic events to occur early in the course of HIT mean that many patients have symptomatic thrombosis at the time that HIT is recognized. Further, there is evidence that isolated HIT defined as a situation where there is a decrease in the platelet count without clinically apparent thrombosis, but is subsequently complicated by thrombosis in one-third to one-half of cases.

"Mechanism of Action and Pharmacology of Unfractionated Heparin"

This article discusses the mechanism of action/pharmacology of unfractionated heparin.

Heparin is a sulfated polysaccharide with a molecular weight range of 3000 to 30 000 Da (mean, 15 000 Da). It produces its major anticoagulant effect by inactivating thrombin and activated factor X (factor Xa) through an antithrombin (AT)-dependent mechanism. Heparin binds to AT through a high-affinity pentasaccharide, which is present on about a third of heparin molecules. For inhibition of thrombin, heparin must bind to both the coagulation enzyme and AT, whereas binding to the enzyme is not required for inhibition of factor Xa. Molecules of heparin with fewer than 18 saccharides lack the chain length to bridge between thrombin and AT and therefore are unable to inhibit thrombin. In contrast, very small heparin fragments containing the pentasaccharide sequence inhibit factor Xa via AT. By inactivating thrombin, heparin not only prevents fibrin formation but also inhibits thrombin-induced activation of platelets and of factors V and VIII.

Clinical Use of Heparin

Heparin is effective for prevention and treatment of venous thrombosis and pulmonary embolism (PE), for prevention of mural thrombosis after myocardial infarction (MI), and for treatment of patients with unstable angina and MI. Although heparin is used to prevent acute thrombosis after coronary thrombolysis, recent reports question the benefits of heparin in this setting when patients are also treated with aspirin.

Treatment

Patients with acute venous thromboembolism (VTE) should receive initial treatment with heparin or LMWH. Based on their superior bioavailability and predictable pharmacokinetic properties, weight-adjusted LMWHs have replaced heparin for the initial treatment of VTE in many centers (see below).

Low-Molecular-Weight Heparins

LMWHs are derived from heparin by chemical or enzymatic depolymerization to yield fragments approximately one third the size of heparin. LMWHs have a mean molecular weight of 4500 to 5000 Da with a distribution of 1000 to 10 000 Da.

All of the anticoagulant, pharmacokinetic, and other biological differences between unfractionated heparin (UFH) and LMWH can be explained by the relatively lower binding properties of LMWH. **Compared with UFH, LMWHs have reduced ability to inactivate thrombin because the smaller fragments cannot bind simultaneously to AT and thrombin. In contrast, because bridging between AT and factor Xa is less critical for anti–factor Xa activity, the smaller fragments inactivate factor Xa almost as well as do larger molecules.** Reduced binding to plasma proteins and cells is responsible for the more predictable dose-response relationship of LMWH, longer plasma half-life (compared with UFH), and lower risk of heparin-induced thrombocytopenia and osteopenia. LMWHs are cleared principally by the renal route.

Prevention of Venous Thrombosis

In general, surgical patients and in medical patients at high risk of venous thrombosis, low doses of LMWH administered SC once daily are at least as effective and safe as low-dose UFH administered SC 2 or 3 times daily. LMWH has become the anticoagulant of choice for the prevention of venous thrombosis during major orthopedic surgery and in anticoagulant-eligible victims of major trauma. The risk of bleeding with LMWH is small and comparable to that with low-dose UFH.

Treatment of VTE

LMWHs are administered in weight-adjusted doses by SC injection and are not monitored. Depending on the LMWH agent, a dose of 100 anti–factor Xa units per kilogram twice daily or of 150 to 200 anti–factor Xa units per kilogram daily is given. Although laboratory monitoring is not usually required, the anti–factor Xa level should be checked in patients with renal insufficiency, morbid obesity, and pregnancy because the pharmacokinetic properties, efficacy, and safety of LMWHs are not well established in these situations.

LMWH preparations are at least as effective and safe as IV heparin for the treatment of deep-vein thrombosis and PE, and the rates of recurrent thromboembolism and major bleeding are similar with all of the LMWH preparations that have been evaluated. (Jack Hirsh; Sonia S. Anand; Jonathan L. Halperin; Valentin Fuster) Correspondence to Jack Hirsh, MD, Hamilton Civic Hospitals Research Center, Henderson General Division, 711 Concessions St, Hamilton, Ontario L8V 1C3, Canada.

HEPARIN & LOW MOLECULAR WEIGHT HEPARIN

http://www.chestjournal.org/content/114/5_Supplement/489

Heparin and Low-Molecular-Weight Heparin Mechanisms of Action, Pharmacokinetics, Dosing Considerations, Monitoring, Efficacy, and Safety

Jack Hirsh, MD, FCCP, Chair; Theodore E. Warkentin, MD; Robert Raschke, MD, MS; Christopher Granger, MD; E. Magnus Ohman, MBBCh; and James E. Dalen, MD, FCCP

(CHEST 1998; 114:489S-510S) DOI 10.1378/chest.114.5_Supplement.489S

Chest 1998;114;489S-510S
Granger, E. Magnus Ohman and James E. Dalen
Jack Hirsh, Theodore E. Warkentin, Robert Raschke, Christopher

LMWH preparations can be administered in either the in-hospital or out-of-hospital setting because they can be administered subcutaneously without the need for laboratory monitoring. When longterm anticoagulant therapy is indicated, heparin or LMWH administration is usually followed by treatment with oral anticoagulants or antiplatelet agents. However, long-term out-of-hospital treatment with heparin or LMWH is used when anticoagulant therapy is indicated in Pregnancy…"

LMWHs are effective and indicated for the prevention of venous thromboembolism, for the treatment of venous thromboembolism, for the treatment of acute pulmonary embolism, and for the early treatment of patients with unstable angina. The levels of evidence and grading of recommendations for the clinical use of heparin and LMWHs are discussed in the chapters that consider the evidence supporting antithrombotic therapy with these agents for the various clinical indications.
In this chapter, the mechanisms of action of heparin and LMWHs, their pharmacokinetics, anticoagulant ef¬ fects, side effects, and laboratory7 monitoring will be

reviewed. The clinical uses of heparin and LMWHs will be summarized briefly since they are discussed in detail in other chapters.

Structure and Mechanism of Action of Heparin

Heparin catalyzes the inactivation of thrombin by ATIII by acting as a template to which both the enzyme and inhibitor bind to form a ternary complex.31517'26-27 In contrast, the inactivation of factor Xa by ATIII/heparin complex does not require ternary complex formation and is achieved by binding of the enzyme to ATIII.2'3-6'7'9'28 Heparin molecules that contain <18 saccharides are unable to bind thrombin and ATIII simultaneously and, therefore, are unable to accelerate the inactivation of thrombin by ATIII, but retain their ability to catalyze the inhibition of factor Xa by ATIII27'2930 (Fig 1). Heparin also catalyzes the inactivation of thrombin by a second plasma cofactor, heparin cofactor II.31 This second anticoagulant effect of heparin is specific for thrombin, it does not require the unique ATIII-binding pentasaccharide, and it requires much higher doses of heparin32-35 than those required to catalyze the activity of ATIII.

Heparin is heterogeneous with respect to molecular size, anticoagulant activity, and pharmacokinetic proper¬ ties.

CHEST/114/5/NOVEMBER, 1998 SUPPLEMENT 489S

rin and

Alliance for the Improvement of Maternity Services (AIMS)

LOVENOX (enoxaparin sodium)

AVENTIS PHARMACEUTICALS

Not FDA approved for pregnancy, labor, delivery or lactation.PDR pg. 713.For the prevention of deep vein thrombosis which may lead to pulmonary embolism. There are no adequate and well controlled studies in pregnant women. There have been a few spontaneous fetal deaths when pregnant women received enoxaparin. For more information from the manufacturer call or write:

Aventis Pharmaceuticals

399 Interpace Parkway

P.O. Box 663
Parsippany, NJ 07054
Direct inquiries to: (800)663-1610

Int J Gynaecol Obstet. 2002 Dec;79(3):299-300. Links

ACOG committee opinion. Safety of Lovenox in pregnancy. Number 276, October 2002. Committee on Obstetric Practice.

American College of Obsterticians and Gynecologists Committee on Obstetric Practice. Committee on Obstetric Practice.

Lovenox (enoxaparin sodium) therapy appears to be safe and efficacious for pregnant women who are candidates for either prophylactic or therapeutic heparin. However, the use of enoxaparin and other low-molecular-weight heparins for therapeutic anticoagulation is not recommended for pregnant women with prosthetic heart valves. Additionally, enoxaparin should be used with caution or discontinued before administration of epidural for pain relief during labor.

Lovenox was deemed to be safe for pregnant women who require either prophylactic or therapeutic heparin, such as Janelle Hill who experienced a deep vein thrombosis.

EXCERPT FROM COMPLAINT

The following was taken from the official complaint in this case regarding alleged negligence by Aventis™ Pharmaceuticals, Inc.

6. The allegations of Paragraphs 1-10 inclusive are incorporated herein as if fully restated herein.

7. During the period February 2003 through July 2003, Janelle Hill, during her pregnancy, was prescribed and injected daily, Lovenox, (enoxaparin sodium), for the treatment of a Deep Venous Thrombosis (DVT) diagnosed during a hospitalization in February and prescribed as a prophylaxis of a hyper-coaguable disorder.

8. Lovenox is an enoxaparin sodium medication manufactured for and distributed by Defendant Aventis Pharmaceuticals, Inc. in the United States.
9. Lovenox was specifically prescribed for Plaintiff Janelle Hill's condition since she was pregnant and the product was represented by Aventis as being appropriate for use in pregnant women.
10. The Plaintiff proceeded to inject the prescription drug twice daily in accordance with her prescription.
11. Upon delivery of the fetus, Plaintiff Savannah Hill, experienced drug exposure to the Lovenox (enoxaparin sodium), resulting in abnormal PT/ PTT levels, thrombocytopenia and intraventricular cranial bleeds; three positive correlative side effects of Lovenox (enoxaparin sodium) exposure.
12. Additionally, the drug exposure to the unborn baby predisposed the infant to a greater degree of severity of birth trauma, given the infant's increased disposition to bleeding.
13. During the labor when the infant became hypoxic, the exposure to the Lovenox (enoxaparin sodium) caused injuries sustained by the infant as well as directly caused a life-threatening condition known as thrombocytopenia, where the infant could not on her own sustain enough platelets to survive and required multiple transfusions.
14. Aventis was negligent in the following particulars:
    a. Aventis is advocating this drug for use in pregnancy despite the fact that there are no adequate and well-controlled studies of safety in pregnant women;
    b. Aventis has failed to provide adequate warnings of the risks of using Lovenox during pregnancy, even though there have been post marketing reports of fetal injuries and fetal deaths when pregnant women received Lovenox injections.
    c. Aventis has been negligent in the testing and marketing of Lovenox;

d. Aventis has been negligent in that they have provided a package insert that is confusing and contradictory;

e. Aventis has been negligent in leading doctors to believe that no testing is necessary to monitor pregnant women who are receiving Lovenox;

f. Aventis has not provided adequate information to doctors prescribing Lovenox to pregnant women for them to know how or when to prescribe Lovenox and to know how to monitor the safety of Lovenox during pregnancy.

g. Aventis has failed to perform adequate post-marketing investigation of fetal injuries and deaths and has failed to adequately inform of the resulting risks from the use of Lovenox during pregnancy

h. Aventis has failed to adequately advise of appropriate dosage information and has provided unsupported recommendations during pregnancy, and has distorted appropriate monitoring necessities.

15. As a result of Defendant Aventis' negligence, your Plaintiffs Janelle Hill and William David Hill have suffered and will continue to suffer medical and rehabilitation expenses, vocational expenses, and care expenses for Savannah Hill, loss of income, both current and in the future, have suffered expenses, mental anguish, and their child shall endure a lifetime of medical expenses and trauma and Plaintiff Savannah Hill has suffered physical deformities including loss of vision, bilateral hearing loss, auditory processing disorder, seizures, Cerebral Palsy, Periventricularleukomalacia, mental retardation, developmental delays, developmental disabilities, loss of future income and enjoyment of life.

LIFE CARE PLAN EVALUATIONS

The following table represents the projected schedule of lifetime medical evaluations that are reasonably foreseeable given her specific medical maladies. I am qualified to offer opinions as to the appropriateness of these projections due to my education, training and experience. I have practiced medicine for 25 years, treating both adults and children. I am certified to perform disability/impairment examinations for children by the Social Security Administration. I have performed hundreds of these evaluations on this pediatric age group. I am qualified to offer opinions as to the chronicity of a child's medical problems and to order medical tests to assess this issue in children. I have done these examinations for the past 20 years. I have also given expert testimony relating to projected lifespan issues. After careful review of the following tables, within a reasonable degree of medical certainty, these projections are accurate and in fact are very conservative.

Source	***Life Care Plan*** ***Projected Evaluations***			
	Evaluation	**Age/Year Initiated through Age/Year Suspended**	**Frequency**	**Cost Per Evaluation**
1.	Physical Therapy Evaluation	5/2009-Life	1x/yr to 18 (pediatric years) 1x/yr 18-Life (adult years)	$130-$720 $144-$353
1.	Occupational Therapy Evaluation	5/2009-Life	1x/yr to 18 (pediatric years)	$144-$453

Source	***Life Care Plan*** ***Projected Evaluations***			
	Evaluation	**Age/Year Initiated through Age/Year Suspended**	**Frequency**	**Cost Per Evaluation**
			1x/yr 18-Life (adult years)	
1.	Speech Therapy Evaluation	5/2009-18/2021	1x/yr	$130-$720
2.	Neuropsychological/ Educational Evaluation	5/2009-21/2024	Every 3 yrs	$2,000 testing, family feedback and report*
3.	Vocational Evaluation	Est. age 22/2025	Estimated 4 x over life	$715-$5,500 for testing and placement in appropriate setting
Rationale/Comments:				
* Could be completed in the school system				
Sources:				
1.	Pediatric pricing: Independent Living 813-963-6923 , All Children's Specialty Care 813-631-5000 Adult pricing: Therapy Station 812-933-1475. University Community Hospital 813-615-7253 & Beth Ingram & Associates			
2.	Neuropsychology Assessment Services 866-284-0211 & Behavioral Neuropsychology 727-341-1402			
3.	Steve Cooley, Vocational Consultant 727-572-0888 and Goodwill Industries 813-874-7077			

Source	***Life Care Plan*** ***Projected Therapeutic Modalities***			
	Therapy	**Age/Year Initiated through Age/Year Suspended**	**Frequency**	**Cost Per Session**
1.	Physical therapy	5/2009-Life	2-3 x/wk through age 18 thereafter allow 6-24 sessions every other year for life	$75-$188 age 5 to 18 $81-$300 ages 18 -life
1.	Occupational therapy	5/2009-Life	2-3 x/wk through age 18 thereafter allow 6-24 sessions every other year for life	$75-$188 age 5-18 $90-$300 ages 18 -life
1.	Speech therapy	5/2009 to 18/2021	2-3 x/wk through age 18 thereafter as needed	$75-$218.30
2.	Counseling - Episodic counseling to address life transitions, peer relationships and adjustment to disability	Est. age 9/2012-Life	*Age 9-101x/wk for 3-6 months Age 12-131x/wk for 3-6 months Age 15-16 1x/wk for 3-6 months Age 17-18 1x/wk for 3-6 months Allowance of 12-16 sessions every 5 yrs	$100-$175
3.	Service Dog Training	5/2009-Life	Replace dog every 8-10 years.	$5,000-$10,000
4.	Service Dog Annual Care	5/2009-Life	Yearly and as needed	Vet Care: Exam $150-$180 incl. vaccines except Bottadella which is $15 1-

Source	***Life Care Plan*** ***Projected Therapeutic Modalities***			
	Therapy	**Age/Year Initiated through Age/Year Suspended**	**Frequency**	**Cost Per Session**
				2x/yr Heart worm test $25 1-2x/yr Stool check $20-$29 1-2x/yr Frontline plus $200/yr License $10/yr(if neutered) $30/yr if not neutered Toenail clipping: $12-15 Microchip-lost and found with each new dog $35-$48 plus registration fee $20 Food $40/mi Allowance of $300-$400/yr Other dog related care items-**See notes below
5.	Therapeutic horseback riding	5/2009 to 18/2021	12-16 sessions- allowance per year	$40 for 45 minute session
6.	Aquatic therapy, special needs swim lessons	5/2009 to 18/2021	18-24 sessions-- allowance per year	$100/mo plus membership fee of $30/yr-private lesson $55-$75 /4wk program-group lessons
7.	Tutorial Assistance	5/2009-21/2024	Annual allowance of 25-40	$30-$60/session

Source	***Life Care Plan*** ***Projected Therapeutic Modalities***			
	Therapy	**Age/Year Initiated through Age/Year Suspended**	**Frequency**	**Cost Per Session**
			sessions/yr	

Rationale/Comments:

Note- when therapy is recommended for a year it refers to a therapy year equaling 48 wks

* These are estimates of frequency and duration of service.

* *Notes-Additional dog care items:

Retractable dog lease, Harness Food/water bowls, Name tag, Chews, Shampoo, Dog bed, Interior car cleaning, Dog crate, Dog gate for home and auto

Sources:

1. Pediatric pricing: Independent Living 813-963-6923 , All Children's Specialty Care 813-631-5000 Adult pricing: Therapy Station 812-933-1475. University Community Hospital 813-615-7253& Beth Ingram & Associates
2. Dr. Wendy Rice 813-969-3878 & Dr. Jacquelyn Flood 813-326-5915
3. All American Dog Training 813-685-6666 Current provider & Elite Professional Dog Training 407-247-1236
4. Country Chase Veterinary 813-814-1814 & Northdale Animal Hospital 813-962-8862, Petsmart
5. Edie Dopking 722-510-3932
6. New Tampa YMCA 813-866-9622
7. Advanced Learning Centers 813-855-6466 & Advantage Tutoring 813-960-3211

Source	***Life Care Plan*** ***Diagnostic Testing / Educational Assessment***				
	Test / Assessment Tool	**Age / Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
	IEP- Individualized Education Plan	5/2009-21/2024	Yearly	Individualized school plan based on special needs	$0 covered under *Individuals with Disabilities Education Improvement Act of 2004* (*IDEA*)
	Special Education Services	5/2009-21/2024	Yearly	Services under IDEA.	$0 covered under *Individuals with Disabilities Education Improvement Act of 2004* (*IDEA*)
1.	Educational Consultant	5/2009-21/2024	Yearly allowance for review of records, meeting with family and attendance at IEP meeting	Educational advocacy	$100-$175/hr allowance of 8-10hrs/yr
Rationale / Comments:					
Sources:					
1.	Dr. Wendy Rice 813-969-3878 & Dr. Jacquelyn Flood 813-326-5915				

Source	***Life Care Plan*** ***Wheelchair Needs***				
	Wheelchair	**Age/Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
1.	Safari tilt convaid wheelchair stroller (purchased in 08)	5/2009	May need to be replaced one time only as it is anticipated that Savannah will be a community ambulatory until she begins aging – see note*	Mobility	$2,670
2.	Light weight manual wheelchair	Est. age 35 yrs/2038	Every 5-7 year	Mobility	$1,040-$1,995
3.	Wheelchair cushion w/cover	Est. age 35 yrs/2038	Every 3 years	Comfort seating	$290-$369 Cover $46-$70
4.	Wheelchair pack	5/2009-Life	One time in 2009 and again at age 35; thereafter every 5 years	Carry items	$25.95
Rationale/Comments:					
*Note-It is anticipated that Savannah will be a community and home ambulator but that as she ages she will require the use of a manual wheelchair.					
Sources:					
1. Spinlife.com 2. Quickie 2 spinlife.com, Invacare 900XT Invacre.com viewed 2-4-09 3. Roho 2008 Price List 4. Allegro.com					

Source	***Life Care Plan*** ***Wheelchair Accessories and Maintenance***				
	Wheelchair Accessory	**Age/Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
	Wheelchair maintenance (first year covered by warranty)	6/2010 until approximately age 10	Yearly	Maintenance	$267/yr
	Wheelchair maintenance (first year covered by warranty)	36/2039	Yearly	Maintenance	$104-$199/yr
Rationale/Comments:					
Sources:					

Source	***Life Care Plan*** ***Aids for Independent Function***				
	Equipment Description	**Age/Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
1.	Hearing aids –see note Needed 5/2009-Life	Estimated age of replacement 7/2010-Life	Every 6-8 yrs as a child and 7-9 yrs in adulthood (after age 18)	Improve hearing	Hearing aid evaluation done before replacement of each new device and every 1-2 years between new devices $90-$106 Ear Molds before replacement of each new device $66 Fitting fee before replacement of each new device $106 Depending on Oticon hearing aid selected VIGO $1,400-$1,600/ aid SUMO DM $1,400-$1,600/ aid TEGO $2,500/aid EPOQ $2,500-$3,200/ aid
2.	Hearing Aid Insurance ESCO Insurance Plan	Estimated age of replacement 7/2010-Life	Yearly	Protection Plus includes: Replacement if your hearing aid is lost , Repair or replacement if your hearing aid	Average of $200/yr

				is accidentally damaged The Platinum Plan includes: Replacement if your hearing aid is lost, Repair for normal wear and tear of your hearing aid including electrical and mechanical failure, Repair or replacement if your hearing aid is accidentally damaged	
3.	Hearing aid batteries (2) Needed 5/2009-Life	5/2009-Life	Change every 1-2 weeks	Power Source	$0.74-$1.31/battery (2) each time changed
4.	Hearing aid storage and cleaning tools	5/2009-Life	Replace every 3 yrs	Maintenance and Storage	Storage device $74.95 Maintenance kit $9.50 contains hearing aid battery tester with key chain, ear wax removal tool and hearing aid cleaning brush.
5.	FM System Needed 5/2009-Life Comes with a one year warranty	5/2009-Life	Replace when hearing aids are replaced-see above	Improves the signal-to-noise ratio	$1,500-$1,700
6.	Computer w/ printer/touch screen, monitor	5/2009-Life	Every 5 yrs	Educational development, communication	$329-$549 computer Screen $399.96-$499.99 Printer $69.99-$99.99
7.	Software for voice recognition and typing	Estimated 8/2011-Life	Every 3 yrs	Educational development, communication	$99

8.	Glasses with protected lenses	5/2009-18/2021	Every 1-2 yrs until age 18	Protect left eye	$300 each
Rationale/Comments:					
Sources:					
1.	All Children's Specialty Care of Tampa 813-631-5000 & Tampa Bay Hearing and Balance Center, De. Zelski USF				
2.	ESCO 800-992-3726				
3.	Walgreens.com and drugstore.com				
4.	Justbecauz.com				
5.	De. Zelski USF				
6.	Dell, Tiger Direct.com, Best Buy				
7.	Dragon speak naturally- Nuance.com				
8.	Family report of previous purchases				

Source	***Life Care Plan*** ***Orthotics/ Prosthetics***				
	Equipment Description	**Age/Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
1.	Shoe inserts	5/2009-Life	Every 3 months	Ambulation	$55
2.	Ankle Foot Orthotics *	5/2009-Life	1x/1-2 yrs until age 16; thereafter 1x/3yr	Ambulation	$1,200-$1,600 for both (estimate)
3.	HEKO knee brace	5/2009-Life	Replace 1-2 x only	Ambulation	$1,000
Rationale/Comments:					
* Savannah currently utilizes Sur Step AFOs but it is anticipated that she will graduate to adult AFOs.					
Sources:					
1.	Family documentation from prior purchases				

Source	***Life Care Plan*** ***Home Furnishings and Accessories***				
	Equipment Description	**Age/Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
1.	Portable ramps	5/2009-Life	Every 10 -15 years	Access	$337.95-$497.95
1.	Hand held shower	5/2009-Life	Replace every 3years	Hygiene	$62.99
1.	Grab bars and installation	5/2009-Life	Replace 5-7 times over life	Safety	$24.99-$36.99 allow for purchase of 3 bars Installation fee: $75 (5-7x over life)
1.	Folding tub bench	5/2009-Life	Replace every 3years	Safety	$159.99
Rationale/Comments:					
Sources:					
1.	Sammons Preston.com				

Source	***Life Care Plan*** ***Medications***		
	Routine Medications	**Purpose**	**Cost**
	No medications are being utilized at this time. In the future Savannah could require a psychostimulant for management of attentional issues.		
Rationale / Comments			
Sources:			

Source	***Life Care Plan*** ***Supplies and Equipment***		
	Supplies/Equipment	**Duration of Need**	**Cost**
1.	Pull ups approximate use 6/day size 5 See Note*	2 years	1.43 ea. estimate 6/day
Rationale/Comments:			
***** Note-it is anticipated that Savannah will be fully potty trained within the next two years.			
Sources:			
1.	CVS		

Source	***Life Care Plan*** ***Home/Facility Care***			
	Home Care	**Age/Year Initiated through Age/Year Suspended**	**Hours/Shifts/Days of Care**	**Cost**
1.	Home care support	5/2009 to age 22/2025	40-45hrs/wk plus 2 full weeks of 24/7 care	Live Out Nanny with experience managing child w/special needs $12-$15/hr $1,800 application fee. If placement doesn't work out within year one the family will not be required to pay the $1,800 again.
2.	**Option 1:** Community-based living with full-time caregiver	22/2025-Life	24/7 live-in	$170-$456/day
3.	Day Program/Sheltered Workshop	22/2025- estimated age 55	5 days /wk for 48-50wks/yr	$30-$95/day (6hrs)
	House cleaning- for heavy cleaning not provided by caregiver	22/2025-Life	1-2x/mo	Allowance of $75-$100/visit .Cost will vary depending on residence selected
4.	Case Management	22/2025-Life	12-14 hrs /yr	$85/hr
Rationale/Comments:				
Sources:				
1. 2. 3. 4.	A Choice Nanny 813-254-8687, Nannies Who Care 727-455-6354 & Nanny Poppinz 813-375-9862 Visiting Angels 813-985-1200, Care First Home Care 813-985-8800, Comfort Keepers 813-935-3600 Quest, Inc 407-218-4300, McDonald Training Center 813-817-2823 & Hillsborough Achievement and Resources Centers 813-951-5655			

Source	***Life Care Plan*** ***Home/Facility Care***			
	Home Care	**Age/Year Initiated through Age/Year Suspended**	**Hours/Shifts/Days of Care**	**Cost**
	Southern Catastrophic Management Services, Inc.			

Source	***Life Care Plan*** ***Home/Facility Care- Residential Placement***			
	Residential Placement	**Age/Year Initiated through Age/Year Suspended**	**Hours/Shifts/Days of Care**	**Cost**
1.	**Option 2:** Supported Living Group Home Placement	22/ 2025-Lifetime	24/7 care and supervision	Association for Retarded Citizens, Tampa $1,600-$4,000/mo inc. room and board, transport Angels Unaware, Tampa $1,144.50-$6,429.21/mo
2.	Day Program/Sheltered Workshop	22/2025- estimated age 55	5 days /wk for 48-50wks/yr	$20-$95/day (6hrs)
3.	Case Management	22/ 2025-Lifetime	12-14 hrs/yr	$85
4.	**Option 3:** Supported Living Residential Placement	22/ 2025-Lifetime	24/7 residential care	Florida Institute for Neurological Rehabilitation, Wauchula $800/day includes medical care, therapies, activities and room and board
Rationale/Comments				
Sources:				
1. 2. 3. 4.	ARC 813-931-3300 & Angels Unaware, Tampa Quest, Inc 407-218-4300, McDonald Training Center 813-817-2823 & Hillsborough Achievement and Resources Centers 813-951-5655 Southern Catastrophic Management Services, Inc. Florida Institute for Neurological Rehabilitation 800-697-5390			

Source	***Life Care Plan*** ***Future Medical Care – Routine***				
1.	Physiatrist	5/2009-Life	2x/yr until age 18; thereafter 1x/yr	Health Management	$60-$88
2.	Neurologist	5/2009-Life	2-4x/yr	Health Management	$125-$376
3.	Ophthalmologist	5/2009-Life	2x/yr until age 8;thereafter 1x/yr	Health Management	$65-$110
4.	ENT/Audiologist	5/2009-Life	1x/yr	Health Management	$40-$97
4.	Hearing Test	5/2009-Life	1x/yr	Health Management	$83-$192
5.	Orthopedist	5/2009-Life	1x/yr	Health Management	$150-$200
6.	Radiology Studies X-rays- pelvis Spine (Scoliosis films)	 Yearly until age 18, thereafter as needed Yearly until age 18	 Yearly until age 18, thereafter as needed Yearly until age 18	Health Management	 $45-$65 $40-$44
7.	Bone density testing	5/2009-Life	3x over life	Diagnostic	$81-$125 incl.

					radiologist fee
8.	Sedated dental care	5/2009-Life	2x/yr	Dental Care	$35 for basic sedation (possible-not included in lifetime totals)
9..	Chiropractor*	5/2009-Life	As needed	Chiropractic treatment	$40
Rationale/Comments:					
* This is not standard of care treatment but it is requested by the family. Savannah is currently seeing Dr. Bain 2 x/wk. Not include in lifetime totals.					
1.	Paul Kornberg, MD 813-228-7696 & Roberto Perez-Millan, MD 813-873-2800				
2.	Pediatric Neurology Associates 813-878-2191, Tampa Neurology Associates 813-872-1548 & West Coast Neurology 813-879-7816				
3.	Tampa Eye Clinic 813-877-2020 & Florida Eye Clinic 813-972-4444				
4.	Tampa Bay ENT & Cosmetic Surgery 813-879-8045 ENT Associates 813-925-5000				
5.	Florida Orthopaedic Institute (813) 978-9700				
6.	SDI Diagnostic Imaging 813-353-9729, Tampa Bay Imaging 813-386-3674, Tampa Diagnostic Center 813-874-7000				
7.	Tower Diagnostic Center 813-874-7000 & SDI Diagnostic Imaging 813-353-3129				
8.	A Safari of Smiles 727-834-8585				
9.	Bain Family Chiropractic 813-907-9898				

Source	*Life Care Plan* *Future Medical Care – Routine*				
	Routine Medical Care	**Age/Year Initiated**	**Frequency of Visits**	**Purpose**	**Cost**
1.	Video EEG (see note)	As needed		Needed if clinical seizure return	$2,248-$7445.65
2.	MRI w/o contrast (see note)	As needed		Needed if clinical seizure return	$401-$420
3.	Mitrochondrial DNA (see note)	As needed		Needed if clinical seizure return	TBD
3.	CPK (see note)	As needed		Needed if clinical seizure return	$23-$44 plus Draw fee $15-$17
Rationale/Comments:					
Note: Mitrochondrial DNA analysis, CPK, MRI w/o contrast and video EEG may be indicated in the future if clinical seizures return- Jose Ferreira, MD note 10/1/08 * The pricing of the Mitrochondrial DNA analysis requires additional information from Dr. Ferreira as there are several different types ranging in cost from $95-$3000					
Sources:					
1. 2.	University Community Hospital 813-971-6000, St. Joseph's Hospital 813-870-4000 & Tampa General Hospital 813-844-7000 SDI Diagnostic Imaging 813-353-9729, Tampa Bay Imaging 813-386-3674 & Tampa Diagnostic Center 813-874-7000				

Source	***Life Care Plan*** ***Transportation***				
	Equipment Description	**Age/ Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
1.	Vehicle modification – retractable step – this item may not be required in the future. It is dependent on the type of car utilized by the family and caregivers	5/2009-Life	Every 5-7 yrs if needed	Access vehicle	$995
Notes:					
Although Savannah will spend increased time in a wheelchair as she ages it is expected that she will be able to					

Source	*Life Care Plan* *Transportation*				
	Equipment Description	**Age/ Year Purchased**	**Replacement Schedule**	**Purpose**	**Cost**
not be necessary.					
Sources:					
1.	Wheelchair Specialties 813-246-9116				

Source	*Life Care Plan* *Therapeutic Recreation*				
	Activity Description	**Social Camps or Programs**	**Age/Year of Purchase or Attendance**	**Replacement or Attendance Schedule**	**Cost**
		Easter Seals Camp	Ages 6-16		$1,326-$2,187 for either 6 or 12 day session, respectively
Rationale/Comments:					
Sources:					

Life Care Plan ***Architectural Renovations***	
Accessibility Needs	**Cost**
Although Savannah will require the use of a wheelchair as she ages it is anticipated that she will be able to walk around her residence. She will require stair railings, grab bars and other devices to ensure safety.	Allowance of $2500 over lifetime

Source	***Life Care Plan*** ***Future Medical Care – Possible Surgical Intervention or Aggressive Treatment Plan***				
	Treatment	**Age/Year Initiated through** **Age/Year Suspended**	**Frequency of treatment**	**Purpose**	**Cost**
1.	Botox injection	5/2009-18/2021 thereafter as needed	2-3 x/yr	Spasticity management	$1,000-$3,000 ea.
2.	Gait analysis	5/2009	1-2 x only	Gait analysis	$2,141.38
3.	Orthopedic surgery- it is possible that Savannah will require orthopedic surgery in the future but the exact type of surgery cannot be identified at this time	Unable to predict		Surgical correction	Unable to predict at this time
Rationale/Comments:					

Source	***Life Care Plan*** ***Future Medical Care – Possible Surgical Intervention or Aggressive Treatment Plan***				
	Treatment	**Age / Year Initiated through Age / Year Suspended**	**Frequency of treatment**	**Purpose**	**Cost**
Sources:					
1.	Paul Kornberg, MD 813-228-7696				
2.	Gait Lab St. Joseph's Hospital –Lauren Rose 813-870-4242				
3.	Source: Paul Kornberg, MD 813-228-7696				

NEGLIGENCE

In the official complaint, the following represents a listing of the alleged areas of negligence by Aventis Pharmaceuticals, Inc. I fully concur with each of these listings regarding the instant case.

COUNT I

(Negligence of Defendant

Aventis Pharmaceuticals, Inc)

During the period February 2003 through July 2003, Janelle Hill, during her pregnancy, was prescribed and injected daily, Lovenox, (enoxaparin sodium), for the treatment of a Deep Venous Thrombosis (DVT) diagnosed during a hospitalization in February and prescribed as a prophylaxis of a hyper-coaguable disorder.

16. Lovenox is an enoxaparin sodium medication manufactured for and distributed by Defendant Aventis Pharmaceuticals, Inc. in the United States.
17. Lovenox was specifically prescribed for Plaintiff Janelle Hill's condition since she was pregnant and the product was represented by Aventis as being appropriate for use in pregnant women.
18. The Plaintiff proceeded to inject the prescription drug twice daily in accordance with her prescription.
19. Upon delivery of the fetus, Plaintiff Savannah Hill, experienced drug exposure to the Lovenox (enoxaparin sodium), resulting in abnormal PT/ PTT levels, thrombocytopenia and intraventricular cranial bleeds; three positive correlative side effects of Lovenox (enoxaparin sodium) exposure.
20. Additionally, the drug exposure to the unborn baby predisposed the infant to a greater degree of severity of birth trauma, given the infant's increased disposition to bleeding.
21. During the labor when the infant became hypoxic, the exposure to the Lovenox (enoxaparin sodium) caused injuries sustained by the infant as well as directly caused a life-threatening condition known as thrombocytopenia, where the infant could not on her own sustain enough platelets to survive and required multiple transfusions.
22. Aventis was negligent in the following particulars:
    a. Aventis is advocating this drug for use in pregnancy despite the fact that there are no adequate and well-controlled studies of safety in pregnant women;
    b. Aventis has failed to provide adequate warnings of the risks of using Lovenox during pregnancy, even though there have been post marketing reports of fetal injuries and fetal deaths when pregnant women received Lovenox injections.
    c. Aventis has been negligent in the testing and marketing of Lovenox;

d. Aventis has been negligent in that they have provided a package insert that is confusing and contradictory;

e. Aventis has been negligent in leading doctors to believe that no testing is necessary to monitor pregnant women who are receiving Lovenox;

f. Aventis has not provided adequate information to doctors prescribing Lovenox to pregnant women for them to know how or when to prescribe Lovenox and to know how to monitor the safety of Lovenox during pregnancy.

g. Aventis has failed to perform adequate post-marketing investigation of fetal injuries and deaths and has failed to adequately inform of the resulting risks from the use of Lovenox during pregnancy

h. Aventis has failed to adequately advise of appropriate dosage information and has provided unsupported recommendations during pregnancy, and has distorted appropriate monitoring necessities.

23. As a result of Defendant Aventis' negligence, your Plaintiffs Janelle Hill and William David Hill have suffered and will continue to suffer medical and rehabilitation expenses, vocational expenses, and care expenses for Savannah Hill, loss of income, both current and in the future, have suffered expenses, mental anguish, and their child shall endure a lifetime of medical expenses and trauma and Plaintiff Savannah Hill has suffered physical deformities including loss of vision, bilateral hearing loss, auditory processing disorder, seizures, Cerebral Palsy, Periventricularleukomalacia, mental retardation, developmental delays, developmental disabilities, loss of future income and enjoyment of life.

The following is the substance of Count II, Breach of Warranty **COUNT II**

(Breach of Warranty of Defendant

Aventis Pharmaceuticals, Inc.)

24. Plaintiffs hereby incorporate the foregoing paragraphs 1- 20 inclusive as if fully restated herein.

25. Aventis, by and through the sale of Lovenox to pregnant women with DVT, expressly and impliedly warranted to the public generally, and to the Plaintiff specifically, that Lovenox was fit for the purposes for which intended. Plaintiff made use of the product as alleged herein, and relied on the express and implied warranties. Contrary thereto, the product was not fit for the intended use, rendering the product unreasonably dangerous. Aventis further breached the express and implied warranties by failure to warn the public in general and this Plaintiff in particular as alleged above, and the improper marketing as to Aventis' failure to warn and failure to provide information necessary to arrive at an informed consent. Beyond that, Aventis specifically misrepresented the product as referred to herein.

26. Aventis' breach of warranties rendered the product unreasonably dangerous and a proximate cause and a producing cause of the occurrence in question and the resulting injuries suffered by Plaintiffs. Further, Aventis' conduct was done knowingly.

27. Defendant Aventis represented that its product, Lovenox, did not cross the placenta, thus representing that it was appropriate for use by pregnant women who suffer from Deep Venous Thrombosis (DVT).

28. Despite the representations that Lovenox was appropriate for use in pregnant women, the medication did cross from Plaintiff Janelle Hill to her infant, Plaintiff Savannah Hill, a/k/a Baby Hill and created complicating, life-threatening conditions at the time of Savannah's birth that have resulted in permanent disabilities.

29. The injuries to Plaintiff Savannah Hill were caused by her exposure to Defendant Aventis' product Lovenox.

30. Therefore, Defendant Aventis breached its express and implied warranties as aforesaid and its warranty of fitness of their product.

As a result of Defendant Aventis' Lovenox (enoxaparin sodium) product, your Plaintiffs Janelle Hill and William David Hill have suffered and will continue to suffer medical and rehabilitation expenses, vocational expenses, and care expenses for Savannah Hill, loss of income, both current and in the future, have suffered expenses, mental anguish, and their child will be facing a lifetime of medical expenses and trauma; and Plaintiff Savannah Hill has suffered physical deformities including loss of vision, bilateral hearing loss, auditory processing disorder, seizures, Cerebral Palsy, Periventricularleukomalacia, mental retardation, developmental delays, developmental disabilities, loss of future income and enjoyment of life.

TO DATE ITEMIZED DAMAGES

The following is an itemized listing of the damages incurred by Savannah Hill resulting from the adverse reaction to Lovenox and its medical sequelae. These medical expenses are reasonable given the degree of Savannah Hill's documented damages. These expenses are related to the effects of Lovenox.

Copy of Itemized Damages as of 6-9-2009(1).xls
SAH SUMMARY
ITEMIZED DAMAGES AS OF 6/6/2008
PATIENT'S NAME: SAVANNAH ANNE HILL

1 MEDICAL COSTS through 6/6/2008:
HEALTHCARE PROVIDER CHARGES
A Ashburn Pediatrics 2,031.00
B Caremark Therapeutic 19,512.90
C Childrens Hosp Healthcare 2,639.00
D Early Intervention SVC 2,190.00
E Fair Oaks Hosp Prof. 485.00
F Fairfax Neonatal Assoc 6,824.00
G INOVA Fairfax Hosp 4,652.50
H Loudoun Medical Grp 2,725.00
I Mary Jo Grote AUD 9,983.50
J Hearing Health Care Center of Manassas, Inc. 9,796.50
K N. VA Ophthalmology Assoc 309.00
L Quest Diagnostics INC 276.04
M Sheridan Childrens Healthc 1,497.00
N Catalina Island Hospital 920.40
O Childrens Hospital & H 14,614.00

P
Other Children Services (See attached EOB Summaries Packet Item 2.) 30,972.67
Q Early Intervention Services 1,320.00
R
Elgin, Virginia- INOVA Fairfax- Pediatric Neurology 397.00
S Afsaneh Hessamfar 2,580.00
T D M Berinstein 7,400.00
U D O Jonas 315.00
V
Gary Magram-INOVA Fairfax-Pediatric Neurosurgery 795.00
W INOVA Fairfax Hosp 55,521.28
X J T Britton 888.00
Y Jay N Greenberg 657.00
Z Linda Tribble 358.00
AA Loudoun Hosp Ctr 10,489.96
AB Loudoun Pathology 637.00
AC Margot Ahronovich 322.00
AD Mark Fowler,MD 2,377.00
AE Medics USA 542.00
AF N VA Ophthalmology Associates 309.00 AG Robert Beck 584.00
AH Robert Hyun 1,480.00
AI Sheridan Childrens Healthc 2,512.00
AJ The Retina Grp of Wash 441.00
AK Department of the Navy 7,963.55
AL AETNA Report 7,383.00
AM
San Diego Regional Center for the Developmentally Disabled 2,513.24
TOTAL MEDICAL EXPENSES: 223,638.80
2 CHILD CARE 15,347.75
AN
La Petite Academy (Amount included in Child Care Expenses and not separately included in total) 8,717.00
3 MISC. MEDS,SUPPLIES, ETC. 43,011.00
4 RESPITE SERV - FAMILY 15,369.41
AO
All People Count in Home Care (Amount included in Respite Service amount and not separately included in total.) 9,156.00
5 AP Moore Children's Center- Easter Seals Camp 648.00
6 CALIFORNIA CHILDREN'S SERVICES 12,660.00
7 LOSS OF INCOME:

Loss of Salary 800,000.00
8 Pain and Suffering
9 Loss of Enjoyment of Life
10
Projected Future Loss (to be included in Life Care Plan)
TOTAL ITEMIZED DAMAGES AS OF 6/6/2008: 1,110,674.96
TOTAL DAMAGES ASSERTED INCLUDING FUTURE CARE AND MEDICAL EXPENSES, PAIN AND SUFFERING and LOSS OF ENJOYMENT OF LIFE 50,000,000.00
Guggino Family Eye Center/ MED3000
Bain Family Chiropractic
St. Jospeh's Hospital: Physical Therapy
St. Jospeh's Hospital: Occupational Therapy

Lifetime Total Costs

I am qualified to offer opinions regarding lifetime costs related to medical negligence due to my education training and experience. I am aware of the general costs of lifetime care in communities similarly situated to the site of the instant Virginia case.

According to the CDC National Vital Statistics Report dated December 28, 2007- U.S. Life Tables, 2004, Volume 56, No. 9 Savannah Hill has a life expectancy of 76.3 years. The figures have not been discounted to present value.

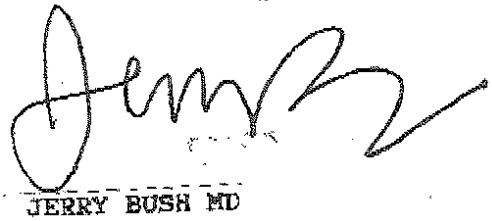
Category	Lifetime Total Costs
Projected Evaluation	$73,821.50
Projected Therapeutic Modalities	$1,031,280.20
Diagnostic Testing/Educational Assessment	$19,800
Wheelchair Needs	$18,094.50
Wheelchair Maintenance/Accessories	$6,870.45
Aids for Independent Function	$102,849.53
Orthotics/Prosthetics	$54,186
Home Furnishings	$6,450.81
Medications	$0
Home Care Home care support to age 22 After age 22 Option 1 Option 2 Option 3	 $564,799.50 $7,312,925.60 $3,225,140 $17,315,600
Routine Medical Care	$101,302
Transportation	$12,653.08
Therapeutic Recreation	$17,565
Architectural Renovations	$2,500
Aggressive Treatment/Surgery	$67,141.38

PROXIMATE CAUSATION

The negligence of Aventis Pharmaceuticals, Inc. related to Savannah Hill was a proximate cause of her current and lifelong severe medical disability.

CONCLUSION

Within a reasonable degree of medical certainty, Savannah Hill will have permanent disability related to the negligence of Aventis Pharmaceuticals, Inc. If not for this negligence, Savannah Hill would not have experienced the noted medical pathology or current projected costs.



JERRY BUSH MD

JERRY W. BUSH, M.D. REFERENCES:

[1] Warkentin T.E.: **Heparin-induced thrombocytopenia**: pathogenesis and management. Br J Haematol 121. (4): 535-555.2003;

[2] Arepally G.M., Ortel T.L.: Clinical practice. **Heparin-induced thrombocytopenia**. N Engl J Med 355. (8): 809-817.2006;

[3] Warkentin T.E.: Management of **heparin-induced thrombocytopenia**: a critical comparison of lepirudin and argatroban. Thromb Res 110. (2–3): 73-82.2003;

[4] Warkentin T.E., Elavathil L.J., Hayward C.P.M., et al: The pathogenesis of venous limb gangrene associated with **heparin-induced thrombocytopenia**. Ann Intern Med 127. (9): 804-812.1997;

[5] Warkentin T.E.: Clinical picture of **heparin-induced thrombocytopenia**. In: Warkentin T.E., Greinacher A., ed. **Heparin-induced thrombocytopenia**, 4th edition Informa Healthcare USA, Inc.New York2007: 21-66.

[6] Warkentin T.E., Levine M.N., Hirsh J., et al: **Heparin-induced thrombocytopenia** in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med 332. (20): 1330-1335.1995;

[7] Warkentin T.E., Roberts R.S., Hirsh J., et al: An improved definition of immune **heparin-induced thrombocytopenia** in postoperative orthopedic patients. Arch Intern Med 163. (20): 2518-2524.2003;

[8] Greinacher A., Farner B., Kroll H., et al: Clinical features of **heparin-induced thrombocytopenia** including risk factors for thrombosis. A retrospective analysis of 408 patients. Thromb Haemost 94. (1): 132-135.2005;

[9] Warkentin T.E., Kelton J.G.: A 14-year study of **heparin-induced thrombocytopenia**. Am J Med 101. (5): 502-507.1996;

[10] Warkentin T.E.: Pseudo-heparin-induced thrombocytopenia. In: Warkentin T.E., Greinacher A., ed. **Heparin-induced thrombocytopenia**, 4th edition Informa Healthcare USA, Inc.New York2007: 261-282.

[11] Warkentin T.E.: Venous limb gangrene during warfarin treatment of cancer-associated deep venous thrombosis. Ann Intern Med 135. (8 Pt 1): 589-593.2001;

[12] Warkentin T.E.: An overview of the **heparin-induced thrombocytopenia** syndrome. Semin Thromb Hemost 30. (3): 273-283.2004;

[13] Kelton J.G., Sheridan D., Santos A., et al: **Heparin-induced thrombocytopenia**: laboratory studies. Blood 72. (3): 925-930.1988;

[14] Warkentin T.E., Sheppard J.I., Moore J.C., et al: Laboratory testing for the antibodies that cause **heparin-induced thrombocytopenia**: how much class do we need?. J Lab Clin Med 146. (6): 341-346.2005;

[15] Greinacher A., Pötzsch B., Amiral J., et al: Heparin-associated thrombocytopenia: isolation of the antibody and characterization of a multimolecular PF4-heparin complex as the major antigen. Thromb Haemost 71. (2): 247-251.1994;

[16] Suh J.S., Aster R.H., Visentin G.P.: Antibodies from patients with heparin-induced thrombocytopenia/thrombosis recognize different epitopes on heparin:platelet factor 4. Blood 91. (3): 916-922.1998;

[17] Greinacher A., Gopinadhan M., Guenther J.U., et al: Close approximation of two platelet factor 4 tetramers by charge neutralization forms the antigens recognized by **HIT** antibodies. Arterioscler Thromb Vasc Biol 26. (10): 2386-2393.2006;

[18] Warkentin T.E., Sheppard J.I., Siguoin C.S., et al: Gender imbalance and risk factor interactions in **heparin-induced thrombocytopenia**. Blood 108. (9): 2937-2941.2006;

[19] Warkentin T.E., Cook R.J., Marder V.J., et al: Anti-platelet factor 4/heparin antibodies in orthopedic surgery patients receiving antithrombotic prophylaxis with fondaparinux or enoxaparin. Blood 106. (12): 3791-3796.2005;

[20] Warkentin TE, Eikelboom JW. Who is (still) getting **HIT**? Chest 2007;131:1620–2.

[21] Lee D.H., Warkentin T.E.: Frequency of **heparin-induced thrombocytopenia**. In: Warkentin T.E., Greinacher A., ed. **Heparin-Induced Thrombocytopenia**, 4th edition Informa Healthcare USA,

Inc.New York2007: 67-116.

[22] Fausett M.B., Vogtlander M., Lee R.M., et al: **Heparin-induced thrombocytopenia** is rare in pregnancy. Am J Obstet Gynecol 185. (1): 148-152.2001;

[23] Warkentin T.E.: Drug-induced immune-mediated thrombocytopenia: from purpura to thrombosis. N Engl J Med 356. (9): 891-893.2007;

[24] Warkentin T.E., Kelton J.G.: Temporal aspects of **heparin-induced thrombocytopenia**. N Engl J Med 344. (17): 1286-1292.2001;

[25] Warkentin T.E., Kelton J.G.: Delayed-onset **heparin-induced thrombocytopenia** and thrombosis. Ann Intern Med 135. (7): 502-506.2001;

[26] Rauova L., Zhai L., Kowalska M.A., et al: Role of platelet surface PF4 antigenic complexes in **heparin-induced thrombocytopenia** pathogenesis: diagnostic and therapeutic implications. Blood 107. (6): 2346-2353.2006;

[27] Warkentin T.E., Jay R.M., Makris M., et al: Platelet-activating anti-platelet factor 4/polyanion antibodies

[31] Warkentin T.E.: Heparin-induced skin lesions. Br J Haematol 92. (2): 494-497.1996;

[32] Warkentin T.E., Hirte H.W., Anderson D.R., et al: Transient global amnesia following intravenous heparin bolus therapy is caused by **heparin-induced thrombocytopenia**. Thromb Haemost 97. (5): 489-491.1994;

[33] Lo G.K., Juhl D., Warkentin T.E., et al: Evaluation of pretest clinical score (4 T's) for the diagnosis of **heparin-induced thrombocytopenia** in two clinical settings. J Thromb Haemost 4. (4): 759-765.2006; without preceding heparin therapy: a transient autoimmune disorder resembling **heparin-induced thrombocytopenia** ("spontaneous **HIT**"). []Blood 108. (11): 311a-312a.2006;

[28] Warkentin T.E.: Think of **HIT**. Hematology Am Soc Hematol Educ Program . 408-414.2006;

[29] Greinacher A., Eichler P., Lietz T., et al: Replacement of unfractionated heparin by low-molecular-weight heparin for postorthopedic surgery antithrombotic prophylaxis lowers the overall risk of symptomatic thrombosis because of a lower frequency of **heparin-induced thrombocytopenia**. Blood 106. (8): 2921-2922.2005;

[30] Warkentin T.E.: Think of **HIT** when thrombosis follows heparin. Chest 130. (3): 631-632.2006;

[34] Warkentin T.E., Sheppard J.I.: Testing for **heparin-induced thrombocytopenia** antibodies. Transfus Med Rev 20. (4): 259-272.2006;

[35] Warkentin T.E.: New approaches to the diagnosis of **heparin-induced thrombocytopenia**. Chest 127. (Suppl 2): 35S-45S.2005;

[36] Lo GK, Sigouin CS, Warkentin TE. What is the potential for overdiagnosis of **heparin-induced thrombocytopenia**? Am J Hematol, in press.

[37] Warkentin T.E., Hayward C.P.M., Smith C.A., et al: Determinants of donor platelet variability when testing for **heparin-induced thrombocytopenia**. J Lab Clin Med 120. (3): 371-379.1992;

[38] Greinacher A., Michels I., Kiefel V., et al: A rapid and sensitive test for diagnosing **heparin-induced thrombocytopenia**. Thromb Haemost 66. (6): 734-736.1991;

[39] Greinacher A, Juhl D, Strobel U, et al. **Heparin-induced thrombocytopenia**: a prospective study on the incidence, platelet-activating capacity and clinical significance of anti-PF4/heparin antibodies of the IgG, IgM, and IgA classes. J Thromb Haemost 2007; May 7 [epub ahead of print].

[40] Warkentin T.E., Greinacher A.: **Heparin-induced thrombocytopenia**: recognition, treatment, and prevention. The seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 126. (Suppl 3): 311S-337S.2004;

[41] Warkentin T.E.: **Heparin-induced thrombocytopenia**: diagnosis and management. Circulation 110. (18): e454-e458.2004;

[42] Chong B.H., Gallus A.S., Cade J.F., et al: Prospective randomized open-label comparison of danaparoid with dextran 70 in the treatment of **heparin-induced thrombocytopenia** with thrombosis: a clinical outcome study. Thromb Haemost 86. (5): 1170-1175.2001;

[43] Lubenow N., Eichler P., Lietz T., et al: Lepirudin in patients with **heparin-induced thrombocytopenia**—results of the third prospective study (HAT-3) and a combined analysis of HAT-1, HAT-2, and HAT-3. J Thromb

Haemost 3. (11): 2428-2436.2005;

[44] Greinacher A., Eichler P., Lubenow N., et al: **Heparin-induced thrombocytopenia** with thromboembolic complications: meta-analysis of two prospective trials to assess the value of parenteral treatment with lepirudin and its therapeutic aPTT range. Blood 96. (3): 846-851.2000;

[45] Lewis B.E., Wallis D.E., Berkowitz S.D., et al: Argatroban anticoagulant therapy in patients with **heparin-induced thrombocytopenia**. Circulation 103. (14): 1838-1843.2001;

[46] Lewis B.E., Wallis D.E., Leya F., et al: Argatroban anticoagulation in patients with **heparin-induced thrombocytopenia**. Arch Intern Med 163. (15): 1849-1856.2003;

[47] Lewis B.E., Wallis D.E., Hursting M.J., et al: Effects of argatroban therapy, demographic variables, and platelet count on thrombotic risks in **heparin-induced thrombocytopenia**. Chest 129. (6): 1407-1416.2006;

[48] Lubenow N., Eichler P., Lietz T., et al: Lepirudin for prophylaxis of thrombosis in patients with acute isolated **heparin-induced thrombocytopenia**: an analysis of 3 prospective studies. Blood 104. (10): 3072-3077.2004;

[49] Greinacher A., Warkentin T.E.: Treatment of **heparin-induced thrombocytopenia**: an overview. In: Warkentin T.E., Greinacher A., ed. **Heparin-induced thrombocytopenia**, 4th edition Informa Healthcare USA, Inc.New York2007: 283-317.

[50] Warkentin T.E.: Should vitamin K be administered when **HIT** is diagnosed after administration of coumarin?. J Thromb Haemost 4. 894-896.2006;